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Remarks

The Office Action mailed January 13, 2003, has been received and reviewed. Claims 10-18 and 24-38 having been canceled, and claims 39-53 having been added, the pending claims are claims 39-53. Reconsideration and withdrawal of the rejections are respectfully requested.

New claim 39 is supported, for example, by claims 10 and 12 (now canceled). New claim 40 is supported, for example, by claim 11 (now canceled). New claims 41 is supported, for example, by claims 24-26 (now canceled). New claims 42-53 are supported, for example, by claims 27-38, respectively (now canceled).

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 10-12 and 24-38 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleged that the term "aliphatic or aromatic residue" is indefinite, as specific amino acids are not recited. Claims 10-12 and 24-38 having been canceled, the rejection is rendered moot. However, to the extent that the rejection applies to new claims 39-53, Applicants respectfully traverse the rejection.

The specification clearly states that "aliphatic residue" means an organic radical having carbon atoms linked in open chains, and that "aromatic residue" means an organic radical that includes an aromatic ring (e.g., an aromatic group, an alkaryl group, or an aralkyl group) (e.g., page 6, lines 26-29). Thus, Applicants respectfully submit that it would be clear to one of skill in the art, based on reading the specification as a whole, that glycine, for example, (which has only hydrogens as substituents on the α -carbon atom), has neither an aliphatic or an aromatic residue as a substituent on the α -carbon atom; and that tyrosine (which has hydrogen and $-\text{CH}_2\text{C}_6\text{H}_4\text{OH}$ as substituents on the α -carbon atom), has an aliphatic or aromatic residue as a substituent on the α -carbon atom.

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Further, the Examiner's question asking if tyrosine is considered to be "polar or aromatic" is not understood, as "polar" is not recited in the claims. Further clarification of the Examiner's question is respectfully requested in the next Official Communication.

Additionally, the Examiner rejected claim 12 for the language "three for 20 minute washes" as being indefinite. Claim 12 having been canceled, the rejection is rendered moot. However, to the extent that the rejection applies to new claim 39, Applicants respectfully traverse the rejection. Applicants respectfully submit that the language in claim 12 clearly conveyed the claimed invention to one of skill in the art. However, in the interest of expediting the prosecution of the present application, the language recited in new claim 39 has been amended as suggested by the Examiner, and the rejection is rendered moot.

Finally, the Examiner rejected claims 29-34 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleged that the language "in register with residues 644-653 of SEQ ID NO:2" is indefinite. Claims 29-34 having been canceled, the rejection is rendered moot. However, to the extent that the rejection applies to new claims 44-49, Applicants respectfully traverse the rejection. Applicants respectfully submit that the language in claims 29-34 clearly conveyed the claimed invention to one of skill in the art. However, in the interest of expediting the prosecution of the present application, the language recited in new independent claims 44 has been amended to recite that "the percentage amino acid identity is determined by placing the TGGNSGSPVF residues of the catalytic domain of the peptidase in register with residues 644-653 of SEQ ID NO:2." Applicants respectfully submit that it would be clear to one of skill in the art that "in register" means that the recited amino acids are aligned, and the rejection is rendered moot.

Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

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Rejection under 35 U.S.C. §112, First Paragraph***Written Description***

The Examiner rejected claims 10, 12-13, and 24-28 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleged that disclosure of a species is insufficient to support a claimed genus. Claims 10, 12-13, and 24-28 having been canceled, the rejection is rendered moot. However, to the extent that the rejection applies to new claims 39 and 41-43, Applicants respectfully traverse the rejection.

Applicants respectfully submit that the isolated nucleic acids recited in independent claims 39 and 41 have been sufficiently described based on physical and/or chemical properties, functional characteristics, and methods of making the isolated nucleic acids to satisfy the written description requirement of 37 C.F.R. §112, first paragraph.

Independent claim 39 recites physical and/or chemical properties. Independent claim 39 recites that "at least about 20 nucleotides of the complement of the nucleic acid hybridize to SEQ ID NO:1 under hybridization conditions of 0.5 M phosphate buffer, pH 7.2, 7% SDS, 10 mM EDTA, at 68°C, followed by three washes for 20 minutes each in 2x SSC, and 0.1% SDS, at 65°C." Applicants respectfully submit that a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims as the hybridization conditions set forth in the claims would be expected to yield structurally similar nucleic acids.

Independent claim 39 further recites function. Independent claim 39 further recites that "the isolated nucleic acid encodes a peptidase, active analog, active fragment, or active modification of the peptidase; . . . the peptidase, active analog, active fragment, and active modification of the peptidase have dipeptidylpeptidase amidolytic activity; and . . . the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the N-terminal end of a target polypeptide

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having an aliphatic or an aromatic residue as a substituent on the α -carbon atom of the second amino acid from the N-terminal end of the polypeptide."

Independent claim 41 recites physical and/or chemical properties. Independent claim 41 recites "[a]n isolated nucleic acid encoding a peptidase; . . . wherein the peptidase comprises a catalytic domain for dipeptidylpeptidase amidolytic activity; and wherein the catalytic domain comprises a sequence comprising residues 543 to 712 of SEQ ID NO:2." Figure 4 shows that residues 543 to 712 of SEQ ID NO:2 includes the sequence TGGNSGSPV that includes the active-site serine residue (underlined) (e.g., specification at page 14, lines 22-27).

Independent claim 41 further recites function. Independent claim 41 further recites "a peptidase having dipeptidylpeptidase amidolytic activity; wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the N-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the α -carbon atom of the second amino acid from the N-terminal end of the polypeptide."

Furthermore, the specification provides examples of how to make the claimed isolated nucleic acids (e.g. page 9, line 22 to page 12, line 26; and page 15, line 2 to page 20, line 25). Further, although not required, the specification includes a description of the actual reduction to practice of making the claimed isolated nucleic acids (e.g. pages 24-27).

Moreover, Applicants respectfully submit that the description of the genus of peptidases by physical and/or chemical properties and by functional characteristics as described herein above, includes sufficient description of a representative number of species.

The M.P.E.P. reads as follows:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice . . . , reduction to drawings . . . , or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between

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function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

M.P.E.P. §2163(II)(A)(3)(a)(ii).

Applicants' Representatives respectfully point out that the M.P.E.P. recites actual reduction to practice of species as only one factor that may satisfy the written description requirement of a claimed genus. Furthermore, the M.P.E.P. recognizes "situations where one species may adequately support a genus" (M.P.E.P. §2163(II)(A)(3)(a)(ii)). Moreover, the "Revised Interim Written Description Guidelines Training Materials" issued by the United States Patent and Trademark Office (<http://www.uspto.gov/web/menu/written.pdf>), recognizes claims where a "single disclosed species is representative of the genus." For example, the guidelines recite the following passages:

The single disclosed species is representative of the genus because reduction to practice of this species, considered along with the defined hybridization conditions and the level of skill and knowledge in the art, are sufficient to allow the skilled artisan to recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus.

and

The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity.

Applicants respectfully submit that in light of the teaching in the present specification, a representative number of adequately described species have been disclosed to satisfy the written description requirement of 37 C.F.R. §112, first paragraph for the genus of peptidases recited in new claims 36, 38-39, and 41-50.

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Thus, Applicants respectively submit that the specification includes a written description sufficient to reasonably convey to one of skill in the art their possession of the claimed invention.

Enablement

The Examiner rejected claims 10, 12-13, and 24-31 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner noted that the specification is enabling for the dipeptidylpeptidase encoded by SEQ ID NO:1, but alleged that the specification does not provide enablement commensurate in scope with the invention as claimed. Claims 10, 12-13, and 24-31 have been canceled, and the rejection is rendered moot. However, to the extent that the rejection applies to new claims 39 and 41-46, Applicants respectfully traverse the rejection.

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P. §2164.04. "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." M.P.E.P. §2164.01(b). "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be *used* in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not *use* the genus as a whole

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without undue experimentation." M.P.E.P. §2164.02, paragraph entitled "WORKING EXAMPLES AND A CLAIMED GENUS" (emphasis added). "[E]ven in unpredictable arts, a disclosure of every operable species is not required." M.P.E.P. §2164.03.

The specification clearly describes methods of making the claimed isolated nucleic acids (e.g. page 9, line 22 to page 12, line 26; and page 15, line 2 to page 20, line 25). Although not required, and as admitted by the Examiner, Applicants have even provided working examples of the claimed isolated nucleic acids (e.g. pages 24-27). Further, the specification provides methods of using the claimed isolated nucleic acids (e.g., page 20, line 26 to page 23, line 20). Notably, the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification.

In spite of the disclosure provided in the specification as noted above, the Examiner asserted that "the specification does not reasonably provide enablement for "any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity." Applicants are not claiming "any nucleic acid molecule encoding any dipeptidylpeptidase activity." The recitations of independent claims 39 and 41 have been discussed in the *Written Description* section herein above.

Independent claim 44 claims isolated nucleic acids by reciting physical and/or chemical properties ("[a]n isolated nucleic acid encoding a peptidase . . . wherein the peptidase comprises a catalytic domain for dipeptidylpeptidase amidolytic activity; wherein the catalytic domain comprises the sequence TGGNSGSPVF (SEQ ID NO:25); wherein the catalytic domain has a percentage amino acid identity of greater than 40% with SEQ ID NO:2; and wherein the percentage amino acid identity is determined by placing the TGGNSGSPVF residues of the catalytic domain of the peptidase in register with residues 644-653 of SEQ ID NO:2").

Independent claim 44 claims isolated nucleic acids by further reciting function ("[a]n isolated nucleic acid encoding a peptidase having dipeptidylpeptidase amidolytic activity; wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the N-terminal end of a target

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polypeptide having an aliphatic or an aromatic residue as a substituent on the α -carbon atom of the second amino acid from the N-terminal end of the polypeptide").

Further, Applicants respectfully reiterate that, as quoted from the M.P.E.P. herein above, *a disclosure of every operable species is not required*. Applicants respectfully submit that one of skill in the art, using the disclosure provided in the specification (including the working examples), would be able to make and use the entire scope of the invention as recited in, for example, independent claims 39, 41, and 44. For example, the specification provides guidance to one of skill in the art in selecting amino acids for substitution into the encoded peptidase (e.g., page 13, line 31 to page 14, line 10). Further, Applicants respectfully submit that one of skill in the art, in view of the present specification, would be enabled to select appropriate amino acids in the peptidase as candidates for substitution (e.g., page 14, line 11 to page 15, line 2).

Moreover, the specification provides one of skill in the art exemplary methods of assaying isolated nucleic acids for amidolytic activity (e.g., page 12, line 27 to page 13, line 25).

Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

Rejection under 35 U.S.C. §102

The Examiner rejected claims 10-13 and 24-38 under 35 U.S.C. §102(a) or (b) over the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208," which the Examiner alleged is admitted prior art by Applicants. Claims 10-13 and 24-38 having been canceled, the rejection is rendered moot. However, to the extent the rejection applies to new claims 39-53, Applicants respectfully traverse the rejection.

For anticipation to occur, a prior art disclosure must put the public in possession of the invention. *See, for example*, M.P.E.P. §2121.01. Applicants respectfully submit that the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208" does not contain an enabling disclosure, and thus, did not put the public in possession of the claimed invention.

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Independent claims 39, 41, 44, and 50 each recite "[a]n isolated nucleic acid." The specification recites that "the term 'isolated' means that a polypeptide or a polynucleotide has been either removed from its natural environment, produced using recombinant techniques, or chemically or enzymatically synthesized" (specification at page 6, lines 8-10).

In contrast, the TIGR database disclosed contigs that are part of the *P. gingivalis* genome in the Unfinished Microbial Genomes database, and Applicants are not claiming such contigs or the unfinished genome. Moreover, the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208" provides no guidance as to which sequence of nucleic acids, if any, might encode a protein. Applicants respectfully submit that the disclosure of the unfinished genome is not an enabling disclosure for making the presently claimed isolated nucleic acids (e.g., independent claims 39, 41, 44, and 50), and thus, fails to anticipate claims 39-53.

The Examiner also requested that Applicants submit any documentation disclosing their discovery that SEQ ID NO:2 was available from the TIGR database and/or when the sequence "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208" was available to the public via the TIGR database. Applicants respectfully direct the Examiner's attention to the declaration submitted by Applicants' Representative, Loren D. Albin, on January 7, 2003.

The Examiner also rejected claim 24 under 35 U.S.C. §102(b) as being anticipated by Simpson et al., *Nature*, 406:151-157 (2000). Applicants note that the Examiner did not supply a copy of the above-referenced document, instead apparently relying on a sequence alignment, a copy of which was attached to the Office Action mailed January 13, 2003. As a courtesy, Applicants are submitting herewith a 1449 form listing Simpson et al. (Exhibit A) along with a copy of Simpson et al. (Exhibit B). It is believed that no fee is due since the document has already been cited by the Examiner. Pursuant to the provisions of M.P.E.P. §609, Applicants further request that a copy of the 1449 form, marked as being considered and initialed by the Examiner, be returned with the next Official Communication. Claim 24 having been canceled, the rejection is rendered moot. However, to the extent the rejection applies to any of the new claims (e.g., claims 39-53), Applicants respectfully traverse the rejection.

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Again, all the new claims recite "[a]n isolated nucleic acid." The specification recites that "the term 'isolated' means that a polypeptide or a polynucleotide has been either removed from its natural environment, produced using recombinant techniques, or chemically or enzymatically synthesized" (specification at page 6, lines 8-10).

In contrast, Simpson et al. disclosed "[t]he genome sequence of the plant pathogen *Xylella fastidiosa*" (title), and Applicants are not claiming the genome sequence of the plant pathogen *Xylella fastidiosa*. Furthermore, Applicants note that the alignment relied on by the Examiner uses the "*hypothetical protein XF1887*" (emphasis added) disclosed by Simpson et al. Moreover, Simpson et al. provides no disclosure to enable one of skill in the art to make or use the presently claimed isolated nucleic acids. Applicants respectfully submit that the disclosure of Simpson et al. is not an enabling disclosure for making the presently claimed isolated nucleic acids, and thus, fails to anticipate any of new claims 39-53.

Applicants respectfully request that the rejections under 35 U.S.C. §102 be reconsidered and withdrawn.